



In the Claims

Please replace all prior versions, and listings, of claims in the application with the following list of claims:

1. (Original) A kit comprising:

a first article having a surface;

a peptide sequence immobilized relative to or adapted to be immobilized relative to the surface, the peptide sequence including a portion of a cell surface receptor that interacts with an activating ligand such as a growth factor to promote cell proliferation, the portion including enough of the cell surface receptor to interact with the activating ligand and the portion free of interchain binding region to the extent necessary to prevent spontaneous binding between portions; and

a candidate drug for affecting the ability of the peptide sequence to bind to other identical peptide sequences in the presence of the activating ligand.

2. (Original) A kit as in claim 1, further comprising a second article having a surface and the peptide sequence immobilized relative to or adapted to be immobilized relative to the surface of the second article.

3. (Original) A kit as in claim 1, wherein the peptide sequence is MGFR.

4. (Original) A method comprising:

providing a peptide including a portion of a cell surface receptor that interacts with an activating ligand such as a growth factor to promote cell proliferation, the portion including enough of the cell surface receptor to interact with the activating ligand and the portion free of interchain binding region to the extent necessary to prevent spontaneous binding between portions;

exposing the peptide to a candidate drug for affecting the ability of the activating ligand to interact with the peptide, and to the activating ligand; and

determining the ability of the candidate drug to prevent interaction of the activating ligand with the peptide.

5. (Original) A method as in claim 4, comprising determining the ability of the candidate drug to prevent interaction of the peptide with other proteins or peptides.

6. (Original) A method as in claim 4, comprising providing a first article having a surface and a plurality of the peptides immobilized relative to or adapted to be immobilized relative to the surface;

exposing the peptides and the surface of the first article to the candidate drug and at least one activating ligand; and

determining the ability of the candidate drug to prevent interaction of the activating ligand with the peptide.

7. (Original) A method as in claim 4, comprising providing a first article having a surface, a second article having a surface, and a plurality of the peptides immobilized relative to or adapted to be immobilized relative to the surfaces of the first and second articles;

exposing the peptides and the surfaces of the first and second articles to the candidate drug and at least one activating ligand; and

determining immobilization of the first and second articles relative to each other.

8. (Original) A method as in claim 4, wherein the step of exposing the peptides to the candidate drug and at least one activating ligand comprises exposing the peptide and the candidate drug to one or both of cell lysate and cell supernatant containing the activating ligand.

9. (Previously Presented) A method as in claim 4, wherein the peptide sequence is the primary sequence of the MUC1 growth factor receptor (PSMGFR).

10. (Original) A method of treating a subject to reduce the risk of or progression of cancer comprising:

administering to a subject who is known to be at risk for cancer or is diagnosed with cancer an agent for inhibiting interaction of an activating ligand with a portion of a cell surface receptor that interacts with the activating ligand to promote cell proliferation.

11. (Original) A method as in claim 10, comprising administering to the subject an agent for inhibiting inductive multimerization of the portion of the cell surface receptor that interacts with the activating ligand to promote cell proliferation.

12. (Original) A method as in claim 10, wherein the cell surface receptor is MUC1

13. (Original) A method as in claim 10, wherein the portion of the cell surface receptor is MGFR.

14. (Original) A method as in claim 10, wherein the portion of the cell surface receptor contains a significant part of the PSMGFR sequence.

15. (Original) A method as in claim 10, comprising administering to the subject an agent for inhibiting dimerization of the portion of the cell surface receptor that interacts with the activating ligand to promote cell proliferation.

16. (Currently Amended) The method of claim 10, wherein the cancers is selected from the group consisting of: MUC1 positive breast, prostate, lung, ovarian, colorectal, and brain cancer.

17. (Original) A method as in claim 10, wherein the activating ligand is a multimer.

18. (Original) The method of claim 10, wherein the activating ligand is a protein with a molecular weight of about 17kD.

19. (Original) The method of claim 10, wherein the activating ligand is a protein with a molecular weight of about 23kD.

20. (Original) The method of claim 10, wherein the activating ligand is a protein with a molecular weight of about 35kD.

21. (Original) The method of claim 10, wherein the activating ligand contains sequences derived from the protein 14-3-3.

22. (Original) The method of claim 10, wherein the activating ligand contains sequences derived from cathepsin D.

23. (Original) The method of claim 10, wherein the activating ligand contains sequences derived from NM23.

24. (Original) The method of claim 10, wherein the activating ligand contains sequences derived from human annexin V.

25. (Original) The method of claim 10, wherein the activating ligand contains sequences derived from beta-lipotropin.

26. (Original) The method of claim 10, wherein the activating ligand is a cleavage product of proopiomelanocortin.

27. (Currently Amended) The method of claim 10, wherein the portion of the cell surface receptor that interacts with the activating ligand to promote cell proliferation comprises at least 12 contiguous amino acids from the sequence
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

28. (Currently Amended) The method of claim 10, wherein ~~the~~ a portion of the cell surface receptor ~~that~~ remains attached to the cell surface after shedding of the cell surface receptor interchain binding region, and the portion that remains attached comprises at least 12 contiguous

amino acids from the peptide sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO: 6).

29. (Previously Presented) The method of claim 10, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

30. (Previously Presented) The method of claim 10, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

31. (Original) A method of treating a subject to reduce the risk or of progression of cancer comprising:

administering to a subject who is known to be at risk of cancer or is diagnosed with cancer, an agent for preventative clustering of portions of cell surface receptors that interact with an activating ligand such as a growth factor to promote cell proliferation.

32. (Original) The method of claim 31, wherein the cell surface receptor is MUC1.

33. (Original) A method as in claim 31, comprising contacting the portions of the cell surface receptor with a molecule that can bind to multiple portions thereby clustering a plurality of the portions.

34. (Previously Presented) A method as in claim 31, wherein the portion is MUC1 Growth Factor Receptor (MGFR).

35. (Currently Amended) A method as in claim 31, wherein the portion contains a significant amount of the primary sequence of the MUC1 growth factor receptor (PF~~S~~MGFR) sequence.

36. (Currently Amended) The method of claim 31, wherein the cancer is selected from the group consisting of MUC1 positive: breast, prostate, lung, ovarian, colorectal, and brain cancer.

37. (Previously Presented) The method of claim 31, wherein the portion of the cell surface receptor comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

38. (Previously Presented) The method of claim 31, wherein the portion of the cell surface receptor comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

39. (Previously Presented) The method of claim 31, wherein the specific binding portion of the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA (SEQ ID NO:7).

40. (Previously Presented) The method of claim 31, wherein the specific binding portion of the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS (SEQ ID NO:6).

41. (Original) A kit comprising:

a species able to become immobilized relative to a shed cell surface receptor interchain binding region; and

a signaling entity immobilized relative to or adapted to be immobilized relative to the species.

42. (Original) A kit as in claim 41, wherein the species binds to a portion of a shed MUC1 receptor that is connected to the interchain binding region.

43. (Original) A kit as in claim 41, wherein the cell surface receptor is MUC1.

44. (Original) The kit as in claim 41, wherein the signaling entity is a colloid particle.
45. (Original) The kit as in claim 41, wherein the signaling entity is not a colloid particle.
46. (Original) The colloid particle as in claim 41, further comprising a colloid particle, wherein the signaling entity is attached to the colloid particle.
47. (Original) A composition comprising:
at least a portion of a shed cell surface receptor interchain binding region; and
a signaling entity immobilized relative to or adapted to be immobilized relative to the portion.
48. (Original) A kit comprising:
a species able to bind to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region; and
a signaling entity immobilized relative to or adapted to be immobilized relative to the species.
49. (Original) A kit as in claim 48, wherein the cell surface receptor is MUC1.
50. (Original) The kit as in claim 48, wherein the signaling entity is a colloid particle.
51. (Original) The kit as in claim 48, wherein the signaling entity is not a colloid particle.
52. (Original) The kit particle as in claim 48, further comprising a colloid particle, wherein the signaling entity is attached to the colloid particle.

53. (Original) The kit as in claim 48, wherein the species able to bind to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a protein of about 17kD.

54. (Original) The kit as in claim 49, wherein the species able to bind to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a protein of about 23kD.

55. (Original) The kit as in claim 49, wherein the species able to bind to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a protein of about 35kD

56. (Original) The kit as in claim 49, wherein the species able to bind to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region contains sequences derived from the protein 14-3-3

57. (Original) The kit as in claim 49, wherein the portion comprises 14-3-3.

58. (Original) The kit as in claim 49, wherein the portion comprises cathepsin D.

59. (Original) The kit as in claim 49, wherein the portion comprises NM23.

60. (Original) The kit as in claim 49, wherein the portion comprises Human annexin V.

61. (Original) The kit as in claim 49, wherein the species able to bind to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region contains at least one sequence derived from beta-lipotropin.

62. (Original) The kit as in claim 49, wherein the species able to bind to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a cleavage product of proopiomelanocortin..

63. (Original) A kit comprising:

 a species able to bind to a portion of a cell surface receptor that includes the interchain binding region; and

 a signaling entity immobilized relative to or adapted to be immobilized relative to the species.

64. (Original) A kit as in claim 63, wherein the cell surface receptor is MUC1.

65. (Original) The kit as in claim 63, wherein the signaling entity is a colloid particle.

66. (Original) The kit as in claim 63, wherein the signaling entity is not a colloid particle.

67. (Original) The colloid particle as in claim 63, further comprising a colloid particle, wherein the signaling entity is attached to the colloid particle.

68. (Original) A peptide species comprising:

 at least a fragment of a sequence that corresponds to that portion of a cell surface receptor that interacts with an activating ligand such as a growth factor to promote cell proliferation, the portion being detached from any cell; and

 an affinity tag.

69. (Original) A peptide species as in claim 68, wherein the affinity tag is connected to the fragment.

70. (Original) A peptide species as in claim 68, wherein the affinity tag defines a portion of a continuous amino acid sequence that includes both the fragment and the affinity tag.

71. (Original) The species of claim 68, wherein the affinity tag is a polyamino acid tag.

72. (Original) The species of claim 68, wherein the affinity tag is a polyhistidine tag.

73. (Original) The species of claim 68, wherein the affinity tag is a GST tag.

74. (Original) The species of claim 68, wherein the affinity tag is biotin.

75. (Original) The species of claim 68, wherein the affinity tag is Thioredoxin.

76. (Currently Amended) The species of claim 68, wherein the affinity tag is selected to bind to a species immobilized with respect to the surface of an article.

77. (Currently Amended) The species of claim 68, further comprising an article having a surface, and a species able to capture the affinity tag immobilized with respect to the surface.

78. (Original) The species of claim 68, wherein the article is a particle.

79. (Original) The species of claim 68, wherein the affinity tag is fastened to the C-terminus of the portion of the receptor.

80. (Original) The species of claim 68, wherein the cell surface receptor is MUC1.

81. (Original) The species of claim 68, wherein the cell surface receptor portion comprises 12 or more contiguous amino acids in the sequence

GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPSAQSGA (SEQ ID NO: 7)

82. (Original) A peptide species as in claim 68, wherein the fragment comprises at least a portion of PSMGFR.

83. (Original) A peptide species as in claim 68, wherein the fragment comprises PSMGFR.

84. (Original) A peptide species as in claim 68, wherein the fragment comprises at least a fragment of the sequence that corresponds to that portion of MUC1 that interacts with an activating ligand such as a growth factor to promote cell proliferation in association with MUC1-dependent tumorigenesis.

85. (Original) A peptide species as in claim 68, wherein the fragment comprises enough of the sequence that corresponds to that portion of MUC1 that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region in association with MUC1-dependent tumorigenesis such that a biomolecule that interacts with that portion of MUC1 that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region in association with MUC1-dependent tumorigenesis interacts with the fragment.

86. (Original) A kit comprising:

a particle; and

at least a fragment of the sequence that corresponds to that portion of a cell surface receptor that interacts with an activating ligand such as a growth factor to promote cell proliferation, the fragment being detached from any cell, fastened to or adapted to be fastened to the particle.

87. (Original) The kit of claim 86, wherein the cell surface receptor is MUC1.

88. (Original) A kit comprising:

an article having a surface; and

a biomolecule that binds to a portion of a cell surface receptor that interacts with an activating ligand such as a growth factor to promote cell proliferation, the biomolecule being fastened to or adapted to be fastened to the surface of the article.

89. (Original) The kit of claim 88, wherein the article comprises a particle.

90. (Original) The kit of claim 88, wherein the cell surface receptor is MUC1.

91. (Original) The kit of claim 88, further comprising:

a second particle; and

a portion of a cell surface receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region, the portion being detached from any cell, fastened to or adapted to be fastened to the second particle.

92. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a protein of about 17kD.

93. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a protein of about 23kD.

94. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a protein of about 35kD.

95. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region contains sequences derived from the protein 14-3-3.

96. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region contains sequences derived from Cathepsin D.

97. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region contains sequences derived from NM23.

98. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region contains sequences derived from human annexin V.

99. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region contains at least one sequence derived from beta-lipotropin.

100. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is a cleavage product of proopiomelanocortin.

101. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region is selected from the group which includes calcimycin, fusaric acid, L- α -methyl-dopa, and etomoxir.

102. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region comprises calcimycin.

103. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region comprises fusaric acid.

104. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region comprises L- α -methyl-dopa.

105. (Original) The kit as in claim 88, wherein the biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region comprises etomoxir.

106. (Original) The composition of claim 88, wherein the biomolecule is derived from a cell line selected from the group consisting of HTB-133, CRL-1504, and CRL-1500.

107. (Original) A method comprising:

exposing a ligand capable of binding with a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region, and an agent capable of blocking said binding, to a candidate drug for disruption of interaction between the ligand and the agent; and

determining disruption of the interaction by the candidate drug.

108. (Original) A method comprising:

exposing a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor interchain binding region which is capable of binding with a ligand, and an agent capable of blocking said binding, to a candidate drug for disruption of interaction between the portion and the agent; and

determining disruption of the interaction by the candidate drug.

109. (Original) A method comprising:

exposing a synthetic drug, and a biological target of the synthetic drug, to a candidate drug which may interact with the biological target to a degree greater than the interaction between the synthetic drug and the target; and

determining disruption of the interaction by the candidate drug.

110. (Original) A method as in claim 109, wherein the synthetic drug is a derivative of fusaric acid.

111. (Original) A method as in claim 109, wherein the synthetic drug is a derivative of L- α -methyl-dopa.

112. (Original) A method as in claim 109, wherein the synthetic drug is a derivative of etomoxir.

113. (Currently Amended) A method for treating a subject having a cancer characterized by the aberrant expression of MUC1, comprising:

administering to the subject fusaric acid in an amount effective to reduce tumor growth.

114. (Original) A method as in claim 113, wherein the subject is otherwise free of symptoms calling for treatment with calcimycin.

115. (Original) A method as in claim 113, wherein the method comprises administering to the subject fusaric acid in an amount effective to block the interaction of a natural ligand and the portion of the MUC1 receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region.

116. (Original) A method as in claim 113, wherein the method comprises administering to the subject fusaric acid in an amount effective to reduce shedding of the interchain binding region of the MUC1 receptor.

117. (Original) The method of 113, wherein the levels of shed interchain binding region are reduced relative to a level measured in a past sample.

118. (Original) The method of 113, wherein the levels of shed interchain binding region are reduced relative to a control sample.

119. (Currently Amended) A method for treating a subject having a cancer characterized by the ~~aberrant~~ expression of MUC1, comprising:

administering to the subject etomoxir in an amount effective to reduce tumor growth.

120. (Original) A method as in claim 119, wherein the subject is otherwise free of symptoms calling for treatment with etomoxir.

121. (Original) A method as in claim 119, wherein the method comprises administering to the subject etomoxir in an amount effective to block the interaction of a natural ligand and the portion of the MUC1 receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region.

122. (Original) A method as in claim 119, wherein the method comprises administering to the subject etomoxir in an amount effective to reduce shedding of the interchain binding region of the MUC1 receptor.

123. (Original) The method of 119, wherein the levels of shed interchain binding region are reduced relative to a level measured in a past sample.

124. (Original) The method of 119, wherein the levels of shed interchain binding region are reduced relative to a control sample.

125. (Currently Amended) A method for treating a subject having a cancer characterized by the ~~aberrant~~ expression of MUC1, comprising:

administering to the subject L- α -methyl-dopa in an amount effective to reduce tumor growth.

126. (Original) A method as in claim 125, wherein the subject is otherwise free of symptoms calling for treatment with L- α -methyl-dopa.

127. (Original) A method as in claim 125, wherein the method comprises administering to the subject L- α -methyl-dopa in an amount effective to block the interaction of a natural ligand and the portion of the MUC1 receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region.

128. (Original) A method as in claim 125, wherein the method comprises administering to the subject L- α -methyl-dopa in an amount effective to reduce shedding of the interchain binding region of the MUC1 receptor.

129. (Original) The method of 125, wherein the levels of shed interchain binding region are reduced relative to a level measured in a past sample.

130. (Original) The method of 125, wherein the levels of shed interchain binding region are reduced relative to a control sample.

131. (Currently Amended) A method for treating a subject having a cancer characterized by the aberrant expression of MUC1, comprising:

administering to the subject calcimycin in an amount effective to reduce tumor growth.

132. (Original) A method as in claim 131, wherein the subject is otherwise free of symptoms calling for treatment with calcimycin.

133. (Original) A method as in claim 131, wherein the method comprises administering to the subject calcimycin in an amount effective to block the interaction of a natural ligand and the portion of the MUC1 receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region.

134. (Original) A method as in claim 131, wherein the method comprises administering to the subject calcimycin in an amount effective to reduce shedding of the interchain binding region of the MUC1 receptor.

135. (Original) The method of 134, wherein the levels of shed interchain binding region are reduced relative to a level measured in a past sample.

136. (Original) The method of 134, wherein the levels of shed interchain binding region are reduced relative to a control sample.

137. (Currently Amended) A method for treating a subject having a cancer characterized by the aberrant expression of MUC1, comprising:
administering to the subject butylindazole in an amount effective to reduce tumor growth.

138. (Original) A method as in claim 137, wherein the subject is otherwise free of symptoms calling for treatment with butylindazole.

139. (Original) A method as in claim 137, wherein the method comprises administering to the subject butylindazole in an amount effective to block the interaction of a natural ligand and the portion of the MUC1 receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region.

140. (Original) A method as in claim 137, wherein the method comprises administering to the subject butylindazole in an amount effective to reduce shedding of the interchain binding region of the MUC1 receptor.

141. (Original) The method of 137, wherein the levels of shed interchain binding region are reduced relative to a level measured in a past sample.

142. (Original) The method of 137, wherein the levels of shed interchain binding region are reduced relative to a control sample.

143. (Currently Amended) A method for treating a subject having a cancer characterized by the aberrant expression of MUC1, comprising:

administering to the subject NS1619 in an amount effective to reduce tumor growth.

144. (Original) A method as in claim 143, wherein the subject is otherwise free of symptoms calling for treatment with NS1619.

145. (Original) A method as in claim 143, wherein the method comprises administering to the subject NS1619 in an amount effective to block the interaction of a natural ligand and the portion of the MUC1 receptor that remains attached to the cell surface after shedding of the cell surface receptor interchain binding region.

146. (Original) A method as in claim 143, wherein the method comprises administering to the subject NS1619 in an amount effective to reduce shedding of the interchain binding region of the MUC1 receptor.

147. (Original) The method of 143, wherein the levels of shed interchain binding region are reduced relative to a level measured in a past sample.

148. (Original) The method of 143, wherein the levels of shed interchain binding region are reduced relative to a control sample.

149. (Original) A method comprising:

exposing a composition selected among calcimycin, butylindazole, NS1619, fusaric acid, L- α -methyl-dopa, and etomoxir, and a biomolecule that binds to a portion of a cell surface receptor that remains attached to the cell surface after shedding of a cell surface receptor

interchain binding region, to a candidate drug which may interfere with interaction between the composition and the biomolecule; and

determining disruption of the interaction by the candidate drug.

150. (Original) A method of treating a subject having cancer or at risk for developing cancer comprising:

administering to the subject an agent that reduces cleavage of a cell surface receptor.

151. (Original) A method of treating a subject having cancer or at risk for developing cancer comprising:

administering to the subject an agent that reduces cleavage of a cell surface receptor interchain binding region from the cell surface.

152. (Original) The method of claim 150, wherein the cell surface receptor is MUC1.

153. (Previously Presented) The method of claim 151, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

154. (Currently Amended) The method of claim 150, wherein the interchain binding region comprises a contiguous amino acid sequence of about 12 to 18 amino acids, within the region of the human MUC1 receptor amino acids 507 through 549 (~~refers to Spicer et al sequence— corresponds to amino acids 1067 through 1100 of Genbank accession # PI5941, PID G547937).~~

155. (Original) The method of claim 150, wherein the interchain binding region comprises a contiguous amino acid sequence of about 12 to 18 amino acids, within the region of the human MUC1 receptor amino acids 525 through 549 (refers to Spicer et al sequence – corresponds to amino acids 1085 through 1109 of Genbank accession # PI5941, PID G547937).

156. (Currently Amended) The method of claim 150, wherein the cancer is selected from the group consisting of MUC1 positive: breast, prostate, lung, ovarian, colorectal, and brain cancer.

157. (Currently Amended) The method of claim 150, wherein the cancer is characterized by the aberrant expression of the MUC1 receptor.

158. (Currently Amended) A method comprising:

determining an amount of cleavage of a cell surface receptor interchain binding region from a cell surface and/or determining an amount of a portion of the cell surface receptor remaining at the surface resulting from such cleavage and accessible to interaction with external agents; and

evaluating indication of cancer or potential for cancer based upon the determining step.

159. (Original) A method as in claim 158, wherein the cell surface receptor is MUC1.

160. (Currently Amended) A method as in claim 158, comprising diagnosing cancer in a subject by determining an amount of shed cell surface receptor interchain binding region in a subject sample and/or determining an amount of MGFR at a cell surface accessible to interaction with external agents; and

evaluating indication of cancer or potential for cancer based upon the determining step.

161. (Original) A method as in claim 158, wherein the evaluating step comprises correlating the amount in a sample to an amount in a control as an indication of cancer or potential for cancer.

162. (Currently Amended) A method as in claim 158, comprising:

determining an amount of cell surface receptor interchain binding region at the surface of a cell from a subject and/or determining an amount of MGFR at a cell surface accessible to interaction with external agents; and

evaluating indication of cancer or potential for cancer based upon the determining step.

163. (Previously Presented) The method of claim 158, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

164. (Original) The method of claim 158, wherein the interchain binding region comprises a contiguous amino acid sequence of about 12 to 18 amino acids, within the region of the human MUC1 receptor amino acids 507 through 549 (refers to Spicer et al sequence – corresponds to amino acids 1067 through 1100 of Genbank accession # PI5941, PID G547937).

165. (Original) The method of claim 158, wherein the interchain binding region comprises a contiguous amino acid sequence of about 12 to 18 amino acids, within the region of the human MUC1 receptor amino acids 525 through 549 (refers to Spicer et al sequence – corresponds to amino acids 1085 through 1109 of Genbank accession # PI5941, PID G547937).

166. (Original) The method of claim 160, wherein the sample is a fluid sample.

167. (Original) The method of claim 160, wherein the sample is blood.

168. (Original) The method of claim 160, wherein the sample is a tissue sample.

169. (Original) The method of claim 160, wherein the sample is a proliferating cell line derived from a subject's cells.

170. (Currently Amended) The method of claim 158, wherein the cancer is characterized by ~~aberrant~~ expression of MUC1.

171. (Currently Amended) The method of claim 158, wherein the amount of interchain binding region is determined by a method selected from the group consisting of MALDI, western blotting, PCR, LCR, rtPCR, cycling probe technology, gel electrophoresis, or antibody-based

assay, magnetic cell sorting, fluorescence activated cell sorting, bead-based assays or an ELISA assay.

172. (Original) The method of claim 158, wherein the amount of interchain binding region is determined by an aggregation assay.

173. (Original) The method of claim 158, wherein the amount of interchain binding region is determined by a colloid-based method such as colloid-colloid or colloid-bead assay.

174. (Original) The method of claim 158, wherein the sample is selected from the group consisting of: a needle biopsy, a tissue specimen, a tissue surface in an intraoperative procedure, and a tissue surface or cellular solution in a minimally invasive procedure such as a laparoscopy.

175. (Original) A method comprising:

determining a site of cleavage of a cell surface receptor in a sample from a subject; and
evaluating an indication of cancer or potential for cancer based upon the determining step.

176. (Original) The method of claim 175, wherein the cell surface receptor is MUC1.

177. (Original) The method of claim 175, wherein the sample is selected from the group consisting of: a needle biopsy, a tissue specimen, a tissue surface in an intraoperative procedure, and a tissue surface or cellular solution in a minimally invasive procedure such as a laparoscopy.

178. (Original) The method of claim 175, wherein the sample is a fluid sample.

179. (Original) The method of claim 175, wherein the sample is blood.

180. (Original) The method of claim 175, wherein the sample is a tissue sample.

181. (Currently Amended) The method of claim 175, wherein the cancer is selected from the group consisting of: MUC1 positive breast, prostate, lung, ovarian, colorectal, and brain cancer.

182. (Currently Amended) A method as in claim 175, wherein the cancer is characterized by the ~~aberrant~~ expression of MUC1.

183. (Currently Amended) The method of claim 175, wherein the site of cleavage is determined by a method selected from the group consisting of MALDI, western blotting, PCR, LCR, rtPCR, cycling probe technology, gel electrophoresis, or antibody-based assay, magnetic cell sorting, ~~flow~~uorescence activated cell sorting, bead-based assays or an ELISA assay.

184. (Original) The method of claim 175, wherein the amount of interchain binding region is determined by a colloid-based method such as colloid-colloid or colloid-bead assay.

185. (Original) A method of determining a cleavage site of a cell surface comprising:
 contacting a cell with an agent that binds specifically to one potential cell surface
receptor cleavage site and another agent that binds specifically to another potential cell surface
receptor cleavage site; and
 comparing the ratio of binding of the two agents to the cell surface.

186. (Original) The method of claim 185, wherein the surface cell receptor is MUC1.

187. (Original) A method of diagnosing a physiological state indicative of cancer or potential for cancer, comprising determining a specific cleavage state of MUC 1 distinguishable from a different cleavage state of MUC1.

188. (Original) A method comprising:
 determining a first amount of cleavage of a cell surface receptor interchain binding region
from a cell surface of a sample from a subject;

determining a second amount of cleavage of a cell surface receptor interchain binding region from a cell surface of a sample from the subject;
comparing the first amount to the second amount.

189. (Original) A method as in claim 188, comprising comparing the first amount to the second amount as an indication of progression of and/or effectiveness of treatment for cancer.

190. (Original) A method as in claim 188, comprising comparing the first amount to the second amount as an indication for administration of an agent for prevention of cancer.

191. (Original) A method as in claim 188, wherein the subject is undergoing treatment for cancer, the method comprising
comparing the first amount to the second amount as an indication of effectiveness of the treatment.

192. (Original) A method as in claim 188, wherein the cell surface receptor is MUC1.

193. (Previously Presented) The method of claim 192, wherein the interchain binding region comprises a contiguous amino acid sequence of at least 12 amino acids from the sequence GFLGLSNIKFRPGSVVVQLTLAFRE (SEQ ID NO:8).

194. (Original) The method of claim 192, wherein the interchain binding region comprises a contiguous amino acid sequence of about 12 to 18 amino acids, within the region of the human MUC1 receptor amino acids 507 through 549 (refers to Spicer et al sequence – corresponds to amino acids 1067 through 1100 of Genbank accession # PI5941, PID G547937).

195. (Original) The method of claim 188, wherein the interchain binding region comprises a contiguous amino acid sequence of about 12 to 18 amino acids, within the region of the human MUC1 receptor amino acids 525 through 549 (refers to Spicer et al sequence – corresponds to amino acids 1085 through 1109 of Genbank accession # PI5941, PID G547937).

196. (Original) The method of claim 188, wherein the sample is a fluid sample.
197. (Original) The method of claim 188, wherein the sample is blood.
198. (Original) The method of claim 188, wherein the sample is a tissue sample.
199. (Currently Amended) The method of claim 188, wherein the cancer is selected from the group consisting of: MUC1 positive breast, prostate, lung, ovarian, colorectal, and brain cancer.
200. (Original) The method of claim 188, wherein the sample is a proliferating cell line derived from a patient's cells.
201. (Currently Amended) The method of claim 188, wherein the amount of interchain binding region is determined by a method selected from the group consisting of MALDI, western blotting, PCR, LCR, rtPCR, cycling probe technology, gel electrophoresis, or antibody-based assay, magnetic cell sorting, ~~flow~~fluorescence activated cell sorting, bead-based assays or an ELISA assay.
202. (Original) The method of claim 188, wherein the amount of interchain binding region is determined by an aggregation assay.
203. (Original) The method of claim 188, wherein the amount of interchain binding region is determined by a colloid-based method such as colloid-colloid or colloid-bead assay.
204. (Original) The method of claim 188, wherein the sample is selected from the group consisting of: a needle biopsy, a tissue specimen, a tissue surface in an intraoperative procedure, and a tissue surface or cellular solution in a minimally invasive procedure such as a laparoscopy.

205. (Original) The method of claim 188, wherein the amount of interchain binding region is determined by a colloid-based method such as colloid-colloid or colloid-bead assay.

206. (Original) The method of claim 188, wherein the sample is selected from the group consisting of: a needle biopsy, a tissue specimen, a tissue surface in an intraoperative procedure, and a tissue surface or cellular solution in a minimally invasive procedure such as a laparoscopy.

207. (Original) A method as in claim 188, comprising determining a first amount of a cell surface receptor interchain binding region at the surface of a cell in a sample from a subject,
determining a second amount of a cell surface receptor interchain binding region at the surface of a cell in a sample from the subject,
comparing the first amount to the second amount.

208. (Original) A method as in claim 188, comprising determining a first amount of a shed cell surface receptor interchain binding region in a sample from a subject,
determining a second amount of a shed cell surface receptor interchain binding region in a sample from the subject,
comparing the first amount to the second amount.

209. (New) A method of diagnosing MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or the risk of such cancer in a subject and treating the subject to reduce the risk of or progression of such cancer, comprising:

determining an amount of cleavage of a MUC1 cell surface receptor interchain binding region from a cell surface and/or determining an amount of a portion of the MUC1 cell surface receptor remaining at the cell surface resulting from such cleavage and accessible to interaction with external agents;

evaluating indication of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or potential for such cancer based upon the determining step and determining that the subject is known to be at risk for such cancer or has such cancer; and

administering to the subject an agent for inhibiting interaction of an activating ligand with the portion of the MUC1 cell surface receptor that remains at the cell surface resulting from cleavage and that interacts with the activating ligand to promote cell proliferation, the portion comprising MGFR and comprising at least 12 contiguous amino acids from the sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA.

210. (New) The method of claim 209, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide, GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA.

211. (New) The method of claim 209, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS.

212. (New) A method of treating a subject to reduce the risk of or progression of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer, comprising:

providing a subject to whom a diagnostic method has been applied comprising determining an amount of cleavage of a MUC1 cell surface receptor interchain binding region from a cell surface and/or determining an amount of a portion of the MUC1 cell surface receptor remaining at the cell surface resulting from such cleavage and accessible to interaction with external agents, and evaluating indication of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or potential for such cancer based upon the determining step and determining that the subject is known to be at risk for such cancer or has such cancer; and

administering to the subject an agent for inhibiting interaction of an activating ligand with the portion of the MUC1 cell surface receptor that remains at the cell surface resulting from cleavage and that interacts with the activating ligand to promote cell proliferation, the portion comprising MGFR and comprising at least 12 contiguous amino acids from the sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA.

213. (New) The method of claim 212, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide,
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPPFSAQSGA.

214. (New) The method of claim 212, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide sequence
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS.

215. (New) A method of diagnosing MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or the risk of such cancer in a subject and treating the subject to reduce the risk of or progression of such cancer, comprising:

determining an amount of cleavage of a MUC1 cell surface receptor interchain binding region from a cell surface and/or determining an amount of a portion of the MUC1 cell surface receptor remaining at the surface resulting from such cleavage and accessible to interaction with external agents;

evaluating indication of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or the potential for such cancer based upon the determining step and determining that the subject is known to be at risk for such cancer or has such cancer; and

administering to the subject an agent for inhibiting dimerization of the portion of the MUC1 cell surface receptor that remains at the cell surface resulting from cleavage and that interacts with the activating ligand to promote cell proliferation, the portion comprising MGFR and comprising at least 12 contiguous amino acids from the sequence
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPPFSAQSGA.

216. (New) The method of claim 215, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide,
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPPFSAQSGA.

217. (New) The method of claim 215, wherein the agent is selected for use in the method by determining its ability to bind to a significant portion of the peptide sequence
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS.

218. (New) A method of treating a subject to reduce the risk of or progression of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer, comprising:

administering to the subject an agent for inhibiting interaction of an activating ligand with a portion of a MUC1 cell surface receptor that remains at the cell surface as a result of cleavage of the MUC1 cell surface receptor interchain binding region from a cell surface and that interacts with the activating ligand to promote cell proliferation, the portion comprising MGFR and comprising at least 12 contiguous amino acids from the sequence
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA.

219. (New) A method of treating a subject to reduce the risk of or progression of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer, comprising:

administering to the subject an agent for inhibiting dimerization of a portion of a MUC1 cell surface receptor that remains at the cell surface as a result of cleavage of the MUC1 cell surface receptor interchain binding region from a cell surface and that interacts with the activating ligand to promote cell proliferation, the portion comprising MGFR and comprising at least 12 contiguous amino acids from the sequence
GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPFPFSAQSGA.

220. (New) A method of diagnosing MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or the risk of such cancer in a subject comprising:

determining an amount of cleavage of a MUC1 cell surface receptor interchain binding region from a cell surface and/or determining an amount of a portion of the MUC1 cell surface receptor remaining at the surface resulting from such cleavage and accessible to interaction with external agents;

evaluating indication of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or the potential for such cancer based upon the determining step and determining that the subject is known to be at risk for such cancer or has such cancer

wherein the portion comprises MGFR and comprises at least 12 contiguous amino acids from the sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPPFSAQSGA.

221. (New) A method of treating a subject to reduce the risk of or progression of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer:

providing a subject to whom a diagnostic method has been applied comprising determining an amount of cleavage of a MUC1 cell surface receptor interchain binding region from a cell surface and/or determining an amount of a portion of the MUC1 cell surface receptor remaining at the surface resulting from such cleavage and accessible to interaction with external agents, and evaluating indication of MUC1 positive breast, prostate, lung, ovarian, colorectal, and/or brain cancer or the potential for such cancer based upon the determining step and determining that the subject is known to be at risk for such cancer or has such cancer; and

administering to the subject an agent for inhibiting dimerization of the portion of the MUC1 cell surface receptor that remains at the cell surface resulting from cleavage and that interacts with the activating ligand to promote cell proliferation, the portion comprising MGFR and comprising at least 12 contiguous amino acids from the sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPPFSAQSGA.

222. (New) The method of claim 158, wherein MGFR comprises at least 12 contiguous amino acids from the sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVSDVPPFSAQSGA.

223. (New) The method of claim 158, wherein MGFR comprises at least 12 contiguous amino acids from the peptide sequence GTINVHDTVETQFNQYKTEAASPYNLTISDVSVS.

224. (New) A method comprising:

determining a first amount of cleavage of at least a portion of a cell surface receptor from a cell surface of a sample from a subject;

determining a second amount of cleavage of at least a portion of a cell surface receptor
from a cell surface of a sample from the subject;
comparing the first amount to the second amount.